REMARKS

In the Final Action dated May 12, 2010, Claims 1-34 were pending[1]. Claims 20 and 22-34 were withdrawn from further consideration as drawn to non-elected claims. Claims 1-19 and 21 were under examination and rejected.

This Response addresses each of the Examiner's rejections. Favorable consideration of all pending claims is therefore respectfully requested.

Claim Amendments

By way of the foregoing amendments, Applicants have amended claim 1 to incorporate features of previous dependent claims 2-4. Claims 5, 7, 12-16 and 18-19 have been amended, *inter alia*, to conform to the amendments made to claim 1 and to delete multiple dependencies. Claims 2-4, 11, 17 and 20-34 have been canceled.

No new matter is introduced. Upon entry of the amendments, claims 1, 5-10, 12-16 and 18-19 will be pending.

35 U.S.C. §102(b) Rejection Based on Hwang

Claims 1-19 and 21 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Hwang et al. (*Current Opinion in Mol. Therapeutics* 1: 471-479, 1999) (hereinafter "Hwang").

The Examiner alleges that Hwang teaches a vaccine construct comprising an avipox virus vector encoding a prostate specific polypeptide. Further, the Examiner also alleges that Hwang teaches advantages of using a xenogeneic form of a prostate specific polypeptide (PAP) in generating antigen specific CTL and antibodies in a case study with rats where the xenogeneic polypeptide stimulates autoimmune prostatitis. The Examiner further alleges that Hwang also

[1] The Examiner has incorrectly identified claims 1-19 and 21 as pending on page 1, Item 4 of the Office Action.

teaches co-expression of immunomodulating protein such as IL-2 with the target prostate tumor specific antigen, and such co-expression allegedly improved the immunotherapeutic effect of poxvirus. Therefore, the Examiner concludes that Hwang teaches all the claimed limitations.

Applicants respectfully disagree.

Applicants submit that a rejection of a claim under 35 U.S.C. §102(b) requires that the single prior art reference disclose every element of the claim. It is axiomatic that there can be no differences between the subject matter of the claim and the disclosure of the prior art. The absence from the reference of any claimed element negates anticipation. Kloster Speedsteel AB v Crucible Inc., 793 F.2d 1565, 1571, 230 USPQ 81, 84 (Fed. Cir. 1986).

In the present case, claim 1 as amended is directed to a vaccine construct, which is characterized by three recited features: (1) the vaccine construct comprises a fowlpox virus vector, (2) the vector expresses a sequence of nucleotides encoding a xenogeneic prostate specific polypeptide or a derivative or analog, and (3) the vector also expresses a sequence of nucleotides encoding an immunostimulatory polypeptide.

Hwang does not teach a vaccine construct that meets all of the three recited features.

Specifically, regarding page 473 and Table 1 relied upon by the Examiner, Applicants note that Hwang discloses a TAA-targeting recombinant fowlpox vector that was able to overcome the negative effects of pre-existing vaccinia immunity (first paragraph col. 1 on page 473). In Table 1, Hwang discloses constructs for use in clinical trials, including a fowlpox:PSA construct, although no results were available at the time for this construct. While the constructs in these passages of Hwang relate to a fowlpox vector (meeting the first recited feature of the claimed construct), none of the constructs of Hwang disclosed therein meets the second recited feature that the vector expresses a sequence of nucleotides encoding a xenogeneic prostate

specific polypeptide or a derivative or analog, nor the third recited feature that the vector also expresses a sequence of nucleotides encoding an immunostimulatory polypeptide.

Regarding the passage bridging columns 1 and 2 on page 474 relied on by the Examiner, the disclosure therein is directed to vaccinia virus vectors, not fowlpox virus vectors as presently claimed. Therefore, the constructs discussed on page 474 of Hwang also do not meet all three of the recited features of the claimed vaccine construct.

Regarding col. 1 of page 472 and col. 1 of page 474 relied on by the Examiner, Hwang refers to vaccination with a xenogeneic prostate antigen and cites Reference No. 16 as evidence. As previously submitted, the xenogeneic prostate specific antigen disclosed in Reference No. 16 (Fong et al., *J. Immunol* 1997, provided with Applicants' IDS dated May 24, 2006), was administered using a vaccinia virus, which is an orthopox, *not* a fowlpox, virus vector. Therefore, the constructs discussed on pages 472 and 474 of Hwang also do not meet all three of the recited features of the claimed vaccine construct.

Regarding pages 475-476 of Hwang relied upon by the Examiner, the discussion therein again was made in the context of vaccinia viruses and *not* avipox viruses.

Applicants therefore respectfully submit that Hwang simply does not disclose a vaccine construct that meets all of the recited features of the claimed vaccine construct. To assert that Hwang anticipates the claimed invention, the Examiner has combined separate elements, which are disclosed in the context of different vaccine constructs, to reconstruct the claimed invention. This reconstruction, which may be an attempt in establishing a *prima facie* obviousness at best (further discussed below), is improperly applied in an anticipation rejection. To conclude that Hwang discloses a vaccine construct that meets each and every element of the

claimed construct is erroneous and unsubstantiated. Accordingly, withdrawal of the rejection under 35 U.S.C. §102(b) based on Hwang is respectfully requested.

35 U.S.C. §102(e) Rejection Based on McNeel

Claims 1-, 3-6, 11-17, 19 and 21 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by McNeel et al. (US2004/01428290A1) (hereinafter "McNeel").

The Examiner alleges that McNeel teaches a genetic vaccine construct comprising an avipox virus vector encoding a xenogeneic prostate specific polypeptide. The Examiner refers to the entire publication, the abstract, and page 10, column 2, paragraphs 0087-0091. The Examiner further alleges that McNeel teaches using fowlpox virus vector expressing "the same antigenic polypeptide (prostatic acid phosphatase (PAP)) as a "boost"" at page 6, paragraph 0046.

Applicants respectfully disagree.

In the first instance, regarding page 10, column 2 (paragraphs 0087-0091) relied on by the Examiner, McNeel describes therein immunization with a *vaccinia* virus construct expressing human PAP, not a vaccine construct that comprises a fowlpox vector, as presently claimed.

Turning to paragraph 0046 referred to by the Examiner, McNeel states:

> "The direction in the field of viral based vaccines is to prime with a virus encoding the antigen and "boost" with the different virus (like adenovirus or fowlpox) encoding the same antigen."

This passage relates very generally to a prior art strategy of boosting with non-vaccinia viral vectors in order to avoid anti-vector immune responses to priming with vaccinia. Applicants respectfully submit that this paragraph does not teach the use of a fowlpox virus vector as the

vaccine, much less a fowlpox virus vector encoding a xenogeneic prostate specific polypeptide, as presently claimed.

Moreover, the vaccine construct, as presently claimed, also requires that the vector co-expresses an immunostimulatory polypeptide. As admitted by the Examiner in the context of the obviousness rejection based on the combination of McNeel and Schlom (discussed below), McNeel does not teach a vaccine construct which co-expresses an immunostimulatory polypeptide.

Accordingly, Applicants respectfully submit that McNeel fails to teach a vaccine construct that meets each and every element of the claimed vaccine construct. Withdrawal of the rejection under 35 U.S.C. §102(e) based on McNeel is respectfully requested.

Additional Discussion of Hwang and McNeel

Even if the Examiner attempts to raise obviousness rejections based on Hwang and on McNeel, respectively, the Examiner must meet his burden to establish *prima facie* obviousness.

Applicants respectfully submit neither Hwang nor McNeel provides any suggestion or expectation of success that human antigen presenting cells would correctly process and present endogenously expressed xenogeneic prostatic acid phosphatase to produce a prostate specific immune response using a fowlpox delivery vector.

In this regard, Applicants note that Hwang is a review article which attempts to summarize the use of recombinant poxviruses in prostate cancer immunotherapy. The authors discuss the small advances made and certain problems observed during preliminary investigation with a number of different proposed immunotherapeutic strategies using recombinant poxviruses. The authors emphasize the observed difficulty in immunizing against self antigens and the uncertainty regarding whether the *in vitro* demonstration of an immune response, either

cellular or humoral, will translate into therapeutic efficacy in prostate cancer patients. The potential advantages and disadvantages of orthopox and avipox viruses are discussed in the article. However, there is no clear indication regarding which theoretical approach will show any promise of success (beyond the preliminary result obtained with vaccinia vectors – see e.g. Fong et al., *J. Immunol* 1997, cited as Reference No. 16 in Hwang on page 472 and 474).

Apart from the difficulties and uncertainties discussed in Hwang, Applicants respectfully submit that vaccinia and avipox viruses have completely different backbones, as well as different abilities to replicate in a host. Those skilled in the art would not have had a reasonable expectation that results achieved with one construct will be representative or predictive of the results with the other.

Additionally, the passage referred to by the Examiner on page 474 of Hwang refers to the published use by Fong et al. (1997) of xenogeneic PAP to break immune tolerance in rats. Fong *et al.* (1997) demonstrates prostate specific inflammation in rats rather than anti-tumor responses. This result was achieved after xenogeneic immunization depending on intravenous administration of a very high level of plaque forming units of replicating vaccinia virus vector. Thus, in Fong *et al.* (1997), a highly immunogenic vector was used at a very high dose that would not be clinically applicable in humans because of the safety risk of intravenous administration of high doses of a replicating pox virus. It cannot be extrapolated from this result that xenogeneic administration to humans using a *non-replicating* avipox virus in place of vaccinia virus would induce immune responses, autoimmune tissue destruction or an anti-tumour immune response.

It was known in the art that it was particularly difficult to induce an immune response against self antigens. Fowlpox was not considered to be as immunogenic as vaccinia or canary

pox. For example, International Publication No. WO 1998/04727 (previously submitted by Applicants in an Information Disclosure Statement dated 24 May, 2006) indicates that it was only possible to elicit partial protection against a measles or rabies virus using a recombinant fowlpox vector. In light of the prior art knowledge in the field including Hwang and McNeel, the skilled artisan would not have been tempted to use a fowlpox vector to administer xenogeneic prostate antigens, as in the present invention, and in any event, there would have been no reasonable expectation of success.

Therefore, the disclosures in Hwang and McNeel, which are directed to vaccinia constructs, among other deficiencies, do not render the presently claimed invention obvious.

35 U.S.C. §103(a) Rejection Based on McNeel And Schlom

Claims 1-8, 11-19 and 21 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over McNeel in view of Schlom et al. (WO 01/95919) (hereinafter "Schlom").

The Examiner admits that McNeel does not teach co-expressing a cytokine gene in an avipox construct. However, the Examiner attempts to cure this deficiency by relying upon Schlom. The Examiner alleges that Schlom teaches a vaccine construct comprising an avipox virus encoding a prostate specific polypeptide and/or a gene encoding a cytokine such as GM-CSF. The Examiner contends that the combination of Schlom and McNeel renders the claims obvious.

However, as submitted above, McNeel fails to teach a fowlpox virus vector encoding a xenogeneic prostate specific polypeptide. McNeel suggests that a *plasmid* vector encoding PAP is preferred as it overcomes the disadvantages of viral vectors including vaccinia vectors. McNeel's disclosure of a fowlpox virus vector in "boosting" does not constitute a teaching, and would not be understood by those skilled in the art to teach, the use of a fowlpox virus vector as

vaccine itself. There was no expectation in the art that xenogeneic immunization of humans using a fowlpox vector could be effective.

Moreover, Applicants submit that the disclosure of McNeel would be considered by the skilled person in the context of a common general knowledge in the art. For example, as stated in Hwang, there was considerable uncertainty regarding whether an avipox vector system could produce an appropriate response. The authors of Hwang emphasize the observed difficulty in immunizing against self antigens and uncertainty regarding whether the *in vitro* demonstration of an immune response will translate into therapeutic efficacy in prostate cancer patients.

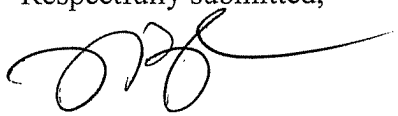
The above fundamental deficiencies of McNeel are not cured by Schlom. Further, the person skilled in the art also would not have been motivated to combine Schlom and McNeel to attempt to arrive at the present invention. The art recognized difficulties associated with fowlpox viruses and would not have added the extra hurdle of producing a xenogeneic response by administering a xenogeneic antigen with a reasonable expectation of success. As evidenced by the prior art, administration of a xenogeneic antigen was neither a routine method to try nor associated with any reasonable expectation of success at the relevant time. It is the present invention that provides the specific combination as claimed.

Accordingly, the present invention is not obvious in view of the combination of McNeel and Schlom. Withdrawal of the rejection under 35 U.S.C. §103(a) based on McNeel and Schlom is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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